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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/573,517	06/05/2006	Laszlo Czollner	SAN1011US	2608
9561	7590	04/09/2009	EXAMINER	
POPOVICH, WILES & O'CONNELL, PA 650 THIRD AVENUE SOUTH SUITE 600 MINNEAPOLIS, MN 55402				COLEMAN, BRENDA LIBBY
1624		ART UNIT		PAPER NUMBER
04/09/2009		MAIL DATE		DELIVERY MODE
				PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/573,517	CZOLLNER ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Brenda L. Coleman	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on \_\_\_\_.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-48 is/are pending in the application.
  - 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_ is/are allowed.
- 6) Claim(s) 1-48 is/are rejected.
- 7) Claim(s) \_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.
 

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. ____ .                                     |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/24/2006 &amp; 4/13/2006</u> .                               | 6) <input type="checkbox"/> Other: ____ .                         |

## DETAILED ACTION

Claims 1-48 are pending in the application.

### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 11-26 and 29-48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. In evaluating the enablement question, several factors are to be considered. *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988); *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

The nature of the invention in the instant case, has claims which embrace substituted 4a,5,9,10,11,12-hexahydrobenzofuro[3a,3,2][2]benzazepines of the instant compounds of the formulae Ia, Ib and Ic wherein the 3-position is substituted with a methoxy group.

HOW TO USE: Claims 11-26 and 29-48 are to a method of treating a disease, which is associated with cholinesterase. Any evidence presented must be

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commensurate in scope with the claims and must clearly demonstrate the effectiveness of the claimed compounds. The scope of the method claims are not adequately enabled solely based on its inhibitory effect on the cholinesterase receptor provided in the specification. Diseases and/or disorder(s) known to be associated with acetylcholinesterase receptors include senile dementia of the Alzheimer's type. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. It is difficult to treat many of the disorders claimed herein. Instant claim language embraces disorders not only for treatment but for **prevention** which is not remotely enabled. It is presumed in the prevention of the diseases and/or disorders claimed herein there is a way of identifying those people who may develop Alzheimer's, etc. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disorders claimed herein.

No screening protocol(s) are ever described. Thus, no evidence of in vitro effectiveness is seen in the specification for one of the instantly claimed 4a,5,9,10,11,12-hexahydrobenzofuro[3a,3,2][2]benzazepine compounds. In general, pharmacological activity is a very unpredictable area. In cases involving physiological activity "the scope of the enablement obviously varies inversely with the degree of unpredictability of the factors involved." *In re Fisher*, 427 F.2d 833, 166 USPQ 18 (CCPA 1970). Since this case involves unpredictable in-vivo physiological activities, the scope of the enablement given in the disclosure presented here was found to be low.

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The specification has no working examples on the use of the substituted 4a,5,9,10,11,12-hexahydrobenzofuro[3a,3,2][2]benzazepines, etc. There must be evidence to justify the contention that the claimed compounds can be useful in the treatment of "Alzheimer's diseases or related conditions of dementia, Parkinson's disease, Huntington's disease (chorea), multiple sclerosis, amyotrophic lateral sclerosis, epilepsy, consequences of stroke, consequences of craniocerebral trauma, effects of diffuse oxygen and nutrient deficiency in the brain, Apoptotic degeneration in neurons, bacterial meningitis, diseases within an apoptotic component, diabetes mellitus, postoperative delirium and/or subsyndromal postoperative delirium, etc.".

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

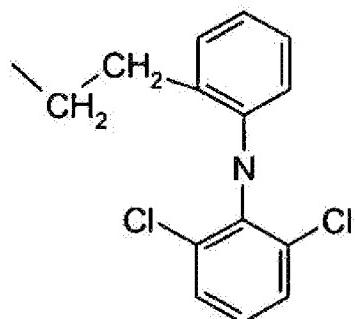
2. Claims 1-7 and 11-48 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "Derivative" which implies more than what is positively recited.
- b. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by general formulae. A formula is not general when all of the variables are defined. Deletion of "general" is suggested.

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c. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the variables R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> within the definition of Z<sub>1</sub> which are defined within the claim.

d. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the moiety which contains a nitrogen atom which is



not valence satisfied.

e. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the definition of the variables R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> where there are no variables R<sub>1</sub>, R<sub>2</sub> and R<sub>3</sub> in the formulae.

f. Claim 1 and claims dependent thereon are vague and indefinite in that it is not known what is meant by the definition of W where W is H. W is divalent and H is monovalent.

g. Claim 2 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "Derivative" which implies more than what is positively recited.

- h. Claim 2 and claims dependent thereon are vague and indefinite in that it is not known what is meant by general formulae. A formula is not general when all of the variables are defined. Deletion of "general" is suggested.
- i. Claim 3 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "Derivative" which implies more than what is positively recited.
- j. Claim 4 and claims dependent thereon are vague and indefinite in that it is not known what is meant by "Derivative" which implies more than what is positively recited.
- k. Claim 7 is vague and indefinite in that it is not known what is meant by general formulae. A formula is not general when all of the variables are defined. Deletion of "general" is suggested.
- l. Regarding claim 20, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).
- m. Regarding claim 38, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

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(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 3-6 and 8-24, 27, 45 and 47 are rejected under 35 U.S.C. 102(b) as being anticipated by Jordis et al., WO 01/74820 (U.S. equivalent 7,166,588). Jordis teaches the compounds, compositions, process of preparing and method of use of the compounds of formulae Ia, Ib, 1, 3, 13, 24, 29, 56, 55, etc. where Z<sub>1</sub> is morpholinylethyl, -CH<sub>2</sub>CH<sub>2</sub>C(O)OCH<sub>2</sub>CH<sub>3</sub>, -C(O)NHCH(CH<sub>3</sub>)<sub>2</sub>, -CH<sub>2</sub>CH<sub>2</sub>CN, -C(S)NHCH<sub>3</sub>, -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>N(CH<sub>3</sub>)<sub>2</sub>, -C(O)NHCH(CH<sub>3</sub>)<sub>2</sub>, -C(SCH<sub>3</sub>) (=NCN), -CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>OH, -C(O)NHC(CH<sub>3</sub>)<sub>3</sub>, pyrimidin-2-yl, 4,6-dichloro-1,3,5-triazin-2-yl, -C(O)NHCH<sub>2</sub>CH<sub>3</sub>, etc.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

4. Claims 1, 3-6, 8-27, 45 and 47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Jordis et al., WO 01/74820 (U.S. equivalent 7,166,588). The generic structure of Jordis encompasses the instantly claimed compounds (see Formula I, (column 1) and for the same uses as claimed herein. Examples such as those found in the table spanning columns 13 through 130, which anticipates the instant invention differs only in the nature of the R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, G<sub>1</sub>, G<sub>2</sub>, G<sub>3</sub> and W substituents. Column 1, line 55 through column 9, line 50 sets forth the definitions of the substituents R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, G<sub>1</sub>, G<sub>2</sub>, G<sub>3</sub> and W. The compounds of the instant invention are

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generically embraced by Jordis in view of the interchange ability of the R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub>, R<sub>5</sub>, G<sub>1</sub>, G<sub>2</sub>, G<sub>3</sub> and W substituents of the 4a,5,9,10,11,12-hexahydrobenzofuro[3a,3,2][2]benzazepine ring system. Thus, one of ordinary skill in the art at the time the invention was made would have been motivated to select for example R<sub>1</sub> is nitro or amino as well as other possibilities from the generically disclosed alternatives of the reference and in so doing obtain the instant compounds in view of the equivalency teachings outlined above.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the “right to exclude” granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1 and 11 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6, 10 and 11 of U.S. Patent No. 7,166,588. Although the conflicting claims are not identical, they are not patentably

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distinct from each other because the compounds and compositions of the instant invention where R<sub>1</sub> is hydrogen or Br; R<sub>2</sub> is hydrogen; R<sub>3</sub> is methoxy; R<sub>4</sub> is H or OH; R<sub>5</sub> is H or OH; G<sub>1</sub> is -CH<sub>2</sub>-; G<sub>2</sub> is -CH<sub>2</sub>-; G<sub>3</sub> is -CH<sub>2</sub>-; and W is N-1,3,5-triazinyl substituted with two Cl.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brenda L. Coleman whose telephone number is 571-272-0665. The examiner can normally be reached on 9:30-6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James O. Wilson can be reached on 571-272-0661. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brenda L. Coleman/  
Primary Examiner, Art Unit 1624